

**Guidance to Industry:
Providing Regulatory
Submissions in Electronic
Format to CDER and CBER**

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March 1, 1999**

Series of guidance

- **General considerations**
- **NDA**
- **Marketing applications to CBER**
- **INA**
- **ANDA**
- **Postmarketing safety reports**
- **...Other types of submissions**

Providing a New Drug Application in Electronic Format

Archival copy – PDF and SAS transport files

Review copy – portion in paper

Field copy – paper

Review aids – electronic files

Relatively rapid change from paper to electronic = major cultural change

To reduce negative impact to reviewers and sponsors, tried to keep electronic submission

- Simple**
- Intuitive**
- Process similar to paper**
- Provide significant advantages over paper**

Simple

- **Reduce reviewer learning curve**
 - Simple, familiar format for accessing documents
 - Allow reviewer to use their own software for analysis of data
- **Limit file formats that are maintained for archiving**
- **Limit different programs supported**
 - Off the shelf programs
- **Limit file formats to be provided**

Simple

Electronic submissions divided into two file types:

Documents

- **Portable Document Format (PDF)**

Datasets

- **SAS Transport files**

Intuitive

- **Divide the submission into files (granularity) based on how the documents and datasets are reviewed**
- **Organize the files based on how the documents are reviewed**

Intuitive

- **Convert each document (or module of a document) into a PDF file**

For example

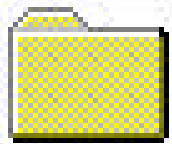
One clinical study report = one pdf file



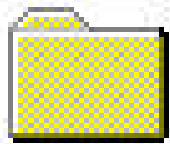
Intuitive

Organizing the collection of PDF files – example- NDA based on FDA form 356h

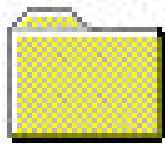
Place all files for each item in the appropriate folder



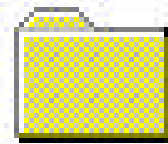
summary



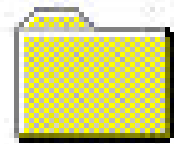
labeling



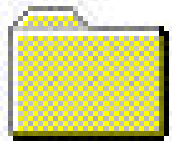
cmc



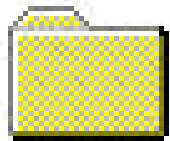
pharmtox



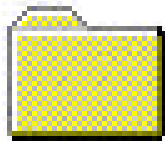
hpbio



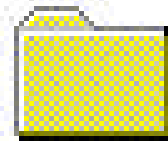
micro



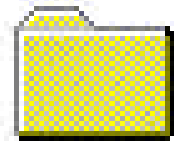
clinstat



crt



crt



other

Process similar to paper

- **Strong cultural bias to the arbitrary size of a piece of paper for narrative reading and writing**

Documents provided in Portable Document Format (PDF)

Electronic paper

- **Maintains look of paper**
 - **Page size**
 - **Format**

Print file change electronic back to paper

Advantages of electronic over paper

- **Electronically copy and paste**
- **Easier access**
- **Faster navigation**
- **Flexible**

**Table of contents electronically linked
for easier navigation**

**Table of contents divided into three
levels:**

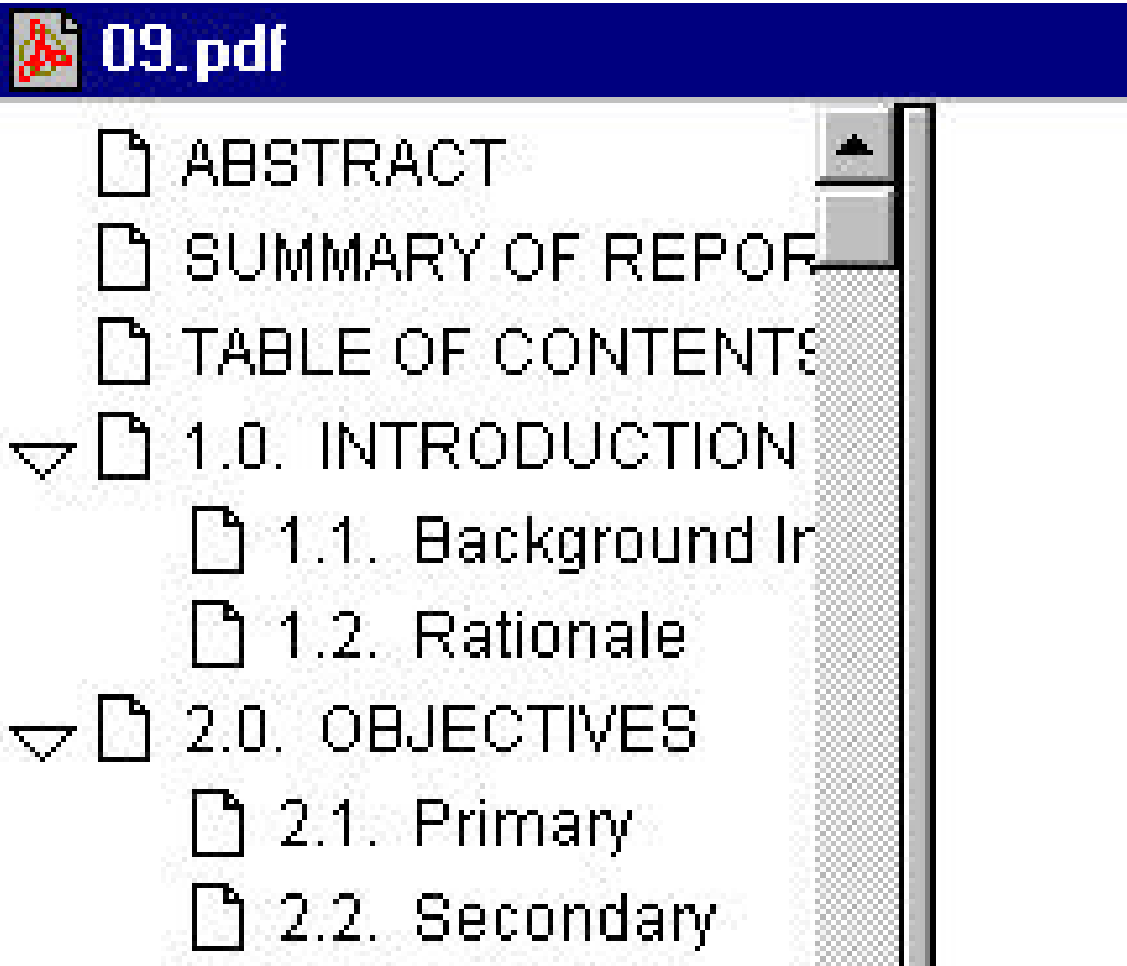
- **Entire submission**
- **Each section**
- **Each document and dataset**

Bookmarks for each section of the document's table of contents

TABLE OF CONTENTS

1.	INTRODUCTION.....
1.1.	Background Information
1.2.	Rationale.....
2.	OBJECTIVES
2.1.	Primary
2.2.	Secondary

Bookmarks



For faster navigation through a document
Hypertext linking to

- **annotations**
- **related sections**
- **references**
- **appendices**
- **tables**
- **figures**

not located on the same page

For faster navigation

A full text index

- **Don't confuse with the table of contents**
- **Index of all words and numbers in the PDF files including the Document information fields**
- **Index consists of a index file (PDX file) and associated files contained in a single folder**



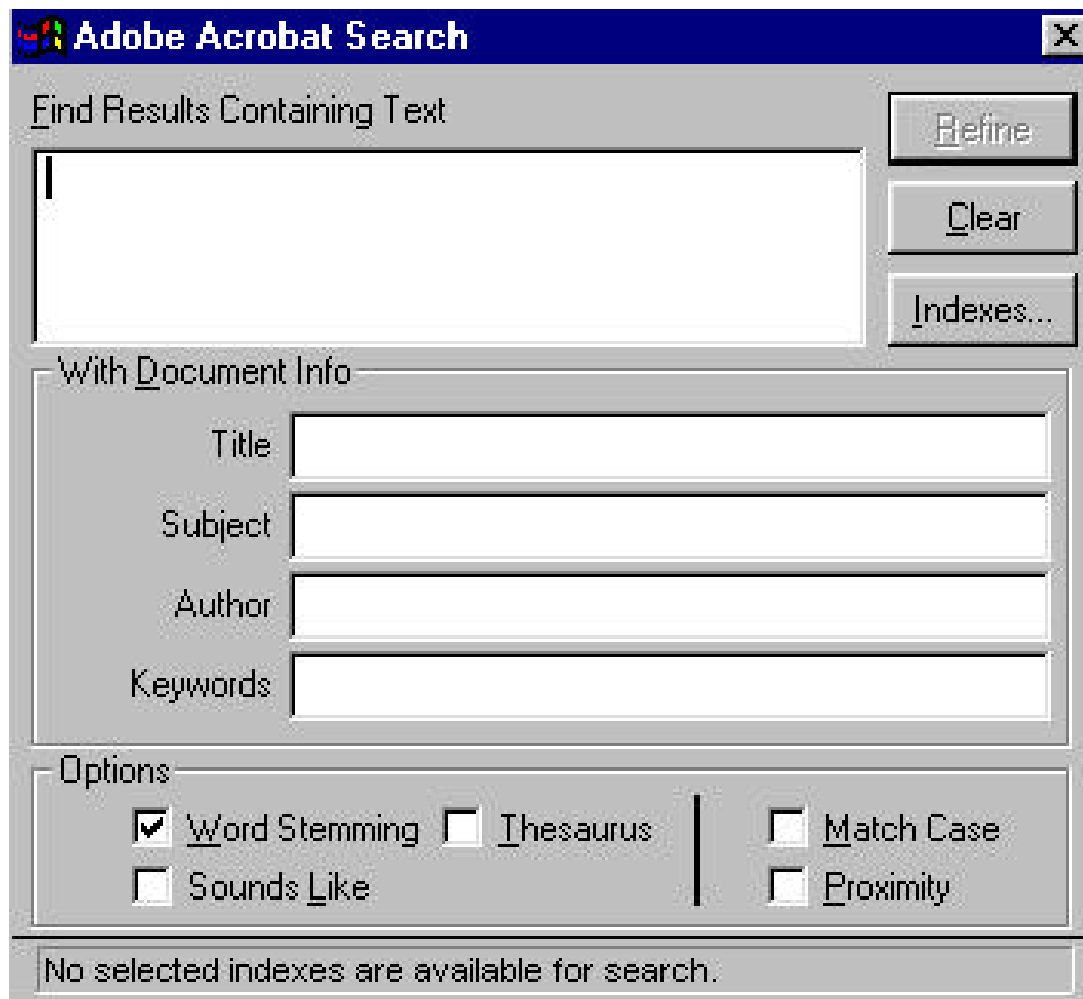
`clinstat.pdx`



`clinstat`

Indexing allows the reviewer to search:

- Text in a document



The image shows a screenshot of the 'Adobe Acrobat Search' dialog box. The title bar is blue with the Adobe logo and the text 'Adobe Acrobat Search'. The main area is light gray. At the top, it says 'Find Results Containing Text' next to a 'Refine' button. Below this is a large text input field with a cursor. To the right of the input field are 'Clear' and 'Indexes...' buttons. Below the input field is a section titled 'With Document Info' containing four input fields: 'Title', 'Subject', 'Author', and 'Keywords'. Below this is an 'Options' section with five checkboxes: 'Word Stemming' (checked), 'Thesaurus', 'Match Case', 'Sounds Like', and 'Proximity'. At the bottom, a status bar says 'No selected indexes are available for search.'

Adobe Acrobat Search

Find Results Containing Text

Refine

Clear

Indexes...

With Document Info

Title

Subject

Author

Keywords

Options

☒ Word Stemming ☐ Thesaurus ☐ Match Case

☐ Sounds Like ☐ Proximity

No selected indexes are available for search.

Flexible

Increased flexibility for how:

- **Submission can be divided**
- **Documents can be accessed**
- **Document can be distributed**

Each document included in a single file or a single folder

Summary:

Electronic submission- tried to keep simple, intuitive, like paper but better